DEPARTMENT OF HEALTH AND HUMAN SERVICES

M986N

Food and Drug Administration
Atlanta District Office
HFI-35

60 8th Street, N.E.
Atlanta, Georgia 30309

June 10, 1997

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Travis Honeycutt
Chief Executive Officer
Isolyser Company
4320 International Blvd., NW
Norcross, Georgia 30093

WARNING LETTER

Dear Mr. Honeycutt:

An inspection of your firm located in Arden, North Carolina, was conducted between April 24 and May 14, 1997. Our investigators found that you are manufacturing and distributing a variety of surgical products. These products are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The investigators documented several significant deviations from the Good Manufacturing Practice for Medical Devices (GMPs) as set forth in Title 21 of the Code of Federal Regulations (21 CFR), Part 820. These deviations cause the devices you manufacture and distribute to be adulterated within the meaning of Section 501(h) of the Act.

You have failed to appropriately validate the sterilization processes in use. You could not provide documented evidence which established a high degree of assurance that the sterilization processes in use are effective and could consistently produce a product meeting its predetermined sterility specifications and quality attributes. Sterilization validation studies were not performed for the [redacted] product line which included gowns, drapes, and towels. These products are sterilized utilizing ethylene oxide (ETO) and gamma radiation. The only evaluation conducted initially involved a determination of product densities. No assessment was conducted of the finished device bioburden. No testing was conducted on finished product for sterility or residuals. No evaluation was conducted to determine if the sterilization process adversely affected the [redacted] material or the devices. The post review of validation effort provided to our investigators was also noted to have significant deficiencies. These reports lacked adequate bioburden analysis, product functionality testing, and residual assessment.

In August 1994 your firm conducted a requalification of the ETO cycle. These results included a positive product sterility test result during one of the half-cycles. In October 1995 your firm performed another requalification in response to this sterility failure. The 1995 protocol included requirements for bioburden analysis, product sterility testing, and residual testing. No data was available on bioburden or sterility testing from this study. Residual testing included results from only half of the samples called for in the protocol.

No revalidation of the ETO cycle has been completed since the above testing performed in 1995. Your firm attempted to revalidate the cycle in 1996 which resulted in positive product sterility samples. This was the last attempt to revalidate this cycle. No written procedures or schedule was available for revalidation of this cycle.

Your firm could provide no documentation that an assessment was made of the ETO residuals in [redacted] products prior to their distribution into the marketplace. The only investigation into residual levels (ethylene chlorohydrin) encountered was conducted in response to a skin irritation complaint in January 1997. In response to that investigation your firm implemented increased testing and longer aeration times. No written formalized investigative report was available of your firm's evaluation as to the cause of these residues and the corrective actions to be implemented.

You have failed to appropriately evaluate the bioburden of your devices to use in the determination of the sterilization cycle to be utilized. Your firm does not have written procedures or an established schedule for the periodic monitoring of device bioburden. The bioburden pre-study on raw materials initiated in 1995 is not completed and data is still being compiled to determine the most difficult to sterilize products. It is not known if this pre-study data is indicative of the bioburden levels on the finished devices as they arrive at the sterilizer. No evaluations have been included of any pre-sterilized finished devices. Sterilization methods are assigned based on bioburden and product densities. In addition to the significant concerns raised as to the method of bioburden determination, some product densities have yet tc be determined, even though sterilization processes have been assigned.

Your firm could provide no data on the quarterly gamma dose audit conducted in the fourth quarter of 1996 or the first quarter of 1997. No audit was conducted in the fourth quarter of 1996 and the results had not been obtained from the 1997 audit. Your firm routinely failed to conduct the dose audits within the specified quarter. Dose audit results were not being received up to three months after the initial request for samples. QA review of the results took up to seven months after the samples were requested.

Your firm had failed to review, evaluate, and maintain all complaints relative to the identity, quality, reliability, safety, effectiveness, and performance of your devices. Review of complaint files revealed a lack of adequate documentation, of the nature of the problems reported, to allow for an appropriate review by your designated review unit or FDA. Complaints were noted to lack dates of initial receipt. Many complaint records failed to include any device failure investigation for devices which apparently had failed product performance specifications after

release. Complaints were not reviewed in a timely manner. Complaint files were noted to be open after six months with no investigation being conducted. The complaint handling system also failed to include any failure analysis of products supplied by foreign manufacturers.

You had failed to provide suitable facilities for the storing of sterile medical devices. The environmental conditions encountered at the public storage facility currently in use were grossly deficient and completely inappropriate for the type of devices you distribute. The warehouse roof was noted to leak in several areas and at least six cases of sterile product had sustained water damage and bore mold growth on the cases. Several sterile product cases were covered with dirt, tar, and debris. At least twelve cases of product were not sealed to help maintain product integrity. Damaged cases of devices were noted throughout the warehouse. The warehouse was in dire need of overall housekeeping improvements. No procedures were available addressing the sanitation requirements of this facility. Your quality assurance unit had failed to assess the adequacy or suitability of this facility.

Your firm failed to follow your procedures pertaining to the operation of the Material Review Board (MRB). Your firm's system for disposition and corrective action for unsuitable goods was not operated as established by procedure. The majority of Material Status Sheets reviewed were incomplete and failed to include any corrective action. Unsuitable materials routinely are not reviewed by the MRB as required. No reviews were performed for at least eleven lots of finished products in quarantine status at the warehouse. Your firm could provide no documentation as the reason these devices were in quarantine status, although they had previously been released for distribution.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. At the close of the inspection, the Inspectional Observations (FDA 483) was issued to and discussed with Malinda K. Graves, Director, RA/QA. A copy of the FDA 483 is enclosed for your review. The specific violations noted in this letter and in the FDA 483 are symptomatic of serious underlying problems in your firm's quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submission of devices to which the GMP deficiencies are reasonably related will be cleared until these violations have been corrected. Also, no request for Certificates For Products for Export will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory actions being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within fifteen (15) days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. We are currently reviewing the May 29 response from Ms. Graves to the FDA 483. We will respond to that letter with any remaining concerns when this review is complete. You may reference that response if you feel it adequately addresses any of the points mentioned in this letter. Your response should be sent to Philip S. Campbell, Compliance Officer, at the address noted in the letterhead.

Sincerely yours,

for Roger E. Kline
Ballard H. Graham, Director
Atlanta District

Enclosure

cc: Thomas Bonner, Jr., VP
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Herndon, Virginia 22070

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